Page 2

- 73. (New) An interferon β polypeptide variant exhibiting an interferon β activity, comprising a variant sequence which differs from the wildtype human interferon β sequence SEQ ID NO:2 in no more than 15 amino acid residues and which comprises one or substitutions relative to SEQ ID NO:2 selected from the group consisting of:
  - (u) Q49N+Q51S/T; and (b) F111N+R113S/T.
- 74. (New) The variant of class; 73, wherein the variant sequence comprises the substitutions Q49N, Q51T, F111N, and R113T.
- 75. (New) The variant of claim 73, wherein the variant sequence further comprises at least one substitution relative to SEQ ID NO:2 selected from: K19R; K33R; and K45R.
- 76. (New) The variant of claim 75, wherein the variant sequence comprises the substitutions K19R, K33R, K45R, Q49N, Q51T, F111N, and R113T.
- 77. (New) The variant of claim 73, wherein the variant sequence further comprises at least one substitution at a position relative to SEQ ID NO:2 selected from: M1; C17; N80; and V101.
- 78. (New) The variant of claim 77, wherein the variant sequence comprises the substitutions C17S, Q49N, Q51T, F111N, and R113T.
- 79. (New) The variant of claim 73, wherein the variant sequence differs from SEQ ID NO:2 in no more than 12 amino acid residues.
- 80. (New) The variant of claim 79, wherein the variant sequence differs from SEQ ID NO:2 in no more than 10 smino acid residues.

Received from < > at 6/17/02 1:25:24 PM [Eastern Daylight Time]

Page 3

81. (New) A polypeptide conjugate exhibiting interferon  $\beta$  activity, which conjugate comprises

- (a) the variant of claim 73, and
- (b) at least one non-polypeptide moiety covalently attached to the variant.
- 82. (New) The conjugate of claim 81, wherein the non-polypeptide moiety is selected from: a polymer molecule, a sugar moiety, a lipophilic compound, and an organic derivatizing agent.
- 83. (New) The conjugate of claim 81, wherein the non-polypeptide moiety and the variant are directly covalently joined to one another, or are indirectly covalently joined to one another.
- 84. (New) The conjugate of claim 82, comprising at least one sugar moiety or at least one polymer molecule covalently attached to the variant.
- 85. (New) The conjugate of claim 84, comprising at least one sugar moiety and at least one polymer molecule covalently attached to the variant.
- 86. (New) The conjugate of claim 85, wherein the variant sequence comprises the substitutions Q49N, Q51T, F111N, and R113T.
- 87. (New) The conjugate of claim 81, wherein the variant sequence further comprises at least one substitution relative to SEQ ID NO:2 selected from: K19R; K33R; and K45R.
- 88. (New) The conjugate of claim 87, wherein the variant sequence comprises the substitutions K19R, K33R, K45R, Q49N, Q51T, F111N, and R113T.

Page 4

89. (New) The conjugate of claim 81, wherein the variant sequence further comprises at least one substitution in a position relative to SEQ ID NO:2 selected from: M1; C17; N80; and V101.

- 90. (New) The conjugate of claim 89, wherein the variant sequence comprises the substitutions C17S, Q49N, Q51T, F111N, and R113T.
- 91. (New) The conjugate of claim 84, wherein the sugar moiety is covalently attached to an asparagine residue of the variant.
- 92. (New) The conjugate of claim 91, wherein the sugar moiety is covalently attached to an asparagine residue of the variant selected from the group consisting Q49N, N80, and F111N.
- 93. (New) The conjugate of claim 84, wherein the polymer molecule is covalently attached to a lysine residue of the variant.
- 94. (New) The conjugate of claim 84, wherein the polymer molecule is covalently attached to the N-terminus of the variant.
- 95. (New) The conjugate of claim 84, wherein the polymer molecule comprises a linear polyethylene glycol or a branched polyethylene glycol.
- 96. (New) An isolated nucleic acid comprising a nucleotide sequence encoding the variant of claim 73.
  - 97. (New) A host cell comprising the nucleic acid of claim 96.
  - 98. (New) An expression vector comprising the nucleic acid of claim 96.

Page 5

- 99. (New) A host cell comprising the expression vector of claim 98.
- 100. (New) The host cell of claim 97 or 99, which host cell is a glycosylating host cell.
- 101. (New) The host cell of claim 100, which glycosylating host cell is a CHO cell, a BHK cell, a HEK293 cell, or an SF9 cell.
- 102. (New) A cell culture comprising the host cell of claim 97 or 99 and a culture medium.
- 103. (New) The cell culture of claim 102, comprising the variant produced by expression of the nucleotide sequence.
- 104. (New) The cell culture of claim 103, wherein the concentration of the variant is at least 800,000 IU/ml of medium.
- 105. (New) A method of producing an interferon β polypeptide variant, the method comprising:

providing a cell culture comprising the host cell of claim 97 or 99 and a culture medium; culturing the cell culture under conditions in which the variant is expressed; and recovering the variant.

- 106. (New) The method of claim 105, wherein the host cell is a glycosylating host cell.
- 107. (New) The method of claim 106, which glycosylating host cell is a CHO cell, a BHK cell, a HEK293 cell, or an SF9 cell.
  - 108. (New) A method for preparing a conjugate, the method comprising: providing the variant of claim 73;

Page 6

contacting the variant with a non-polypeptide moiety under conditions conducive for conjugation; and

recovering the conjugate.

109. (New) A method for preparing a conjugate, the method comprising: providing a cell culture comprising the host cell of claim 97 or 99 and a culture medium; culturing the cell culture under conditions in which the variant is expressed; recovering the variant;

contacting the variant with a non-polypeptide moiety under conditions conducive for conjugation; and

recovering the conjugate.

- 110. (New) The method of claim 109, wherein the host cell is a glycosylating host cell.
- 111. (New) A composition comprising the variant of claim 73 or the conjugate of claim 81 and a pharmaceutically acceptable diluent, carrier, excipient or adjuvant.
- 112. (New) A method for treating a mammal with a disease for which interferon  $\beta$  is a useful treatment, comprising administering to the mammal an effective amount of the composition of claim 111.
  - 113. (New) The method of claim 112, wherein the disease is multiple sclerosis.
- 114. (New) A method for treating a mammal having circulating antibodies against interferon  $\beta$  1a or 1b, which method comprises administering to the mammal an effective amount of the composition of claim 111.
  - 115. The method of claim 112 or 114, wherein the mammal is a human.